# PEER REVIEW HISTORY

This paper was submitted to a another journal from BMJ but declined for publication following peer review. The authors addressed the reviewers' comments and submitted the revised paper to BMJ Open. The paper was subsequently accepted for publication at BMJ Open.

(This paper received three reviews from its previous journal but only two reviewers agreed to published their review.)

## ARTICLE DETAILS

| TITLE (PROVISIONAL) | Emergency Hospital Care for Adults with Suspected Seizures in the NHS in England 2007-2013: A Cross-Sectional Study |
| --- | --- |
| AUTHORS | Dickson, Jon Mark; Jacques, Richard; Reuber, Markus; Hick, Julian; Campbell, Michael Joseph; Morley, Rebeka; Grünewald, Richard A |

## VERSION 1 – REVIEW

| REVIEWER | Katherine Hunold Buck<br>The Ohio State University United States of America |
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| REVIEW RETURNED | 25-Apr-2018 |

| GENERAL COMMENTS | The authors utilize a large database in England to describe the healthcare burden by visits for suspected seizures. The manuscript is well-written and figures intentional to display the data in a meaningful way.<br><br>Specific questions and comments are included below:<br><br>General:<br>How should or could these results inform patient care and future investigations?<br><br>What are the public health implications of these results?<br><br>What is the applicability of these results outside the UK health system?<br><br>Methods:<br>How did you choose the timer period of April 1, 2007 – March 31, 2013?<br><br>How many PCTs were excluded when you excluded the top and bottom 10% based on z-score?<br><br>Results / Conclusions: |
| --- | --- |

How do your results for number of ED epilepsy visits and admissions for neurologic conditions compare to previous data? Specifically, when you compare it, does it appear you choose your population correctly?

Are there identifiable drivers for the geographic variability in admissions? Mapping the rates may be helpful to visually identity. If so, did you consider geographic weighted regression to test these associations?

Do the PCTs identified as outliers cluster geographically?

| REVIEWER | Dr Pete Dixon<br>Research Associate University of Liverpool, UK |
|---|---|
| REVIEW RETURNED | 28-Apr-2018 |

| GENERAL COMMENTS | Thank you for the opportunity to review this interesting paper. My comments are as follows.<br><br>Page 4 – line54: it would be useful to know the method used to define emergency/unscheduled admissions from the HES in-patient database, i.e. which variable field and which values within it. In addition, it is not clear if the data analysis has been undertaken on episodes or spells, and if the latter, was it the initial episode or the final episode which was used to extract the primary diagnosis? It is not uncommon for the primary diagnosis to change as the spell progresses, so this is an important issue to clarify.<br><br>Page 5 – lines 19/20: for consistency with the preceding two definitions of searches, it should state if the admissions for dissociative convulsions were on primary diagnosis only.<br><br>Page 5 – lines 23/24: for clarity it should state from which list the stroke/TIA codes were excluded.<br><br>Page 5 – line 28: from where was the data on costs derived?<br><br>Page 5 – line 48: "… then PCT that are truly outlying …" should read "… then PCTs that are truly outlying …"<br><br>Page 6 – lines 21/22: the reporting of the number of dissociative convulsions as a percentage of the suspected seizures is confusing. As it stands, the wording makes it sound as though the dissociative convulsion's code is part of the epilepsy code, when it is made clear in the methods section that it is separate. This should be re-worded to avoid any confusion.<br><br>Page 6 – 'Geographical variability in admissions' section: It is stated that there are five PCTs which are identified as outliers, and refers to the funnel plots in figure C. However, the funnel plots refer to the three separate groups of admission (seizure, neurological conditions and dissociative convulsions), and it is not clear if those PCTs are considered outliers for all, one, or a combination of those conditions.<br><br>Page 7 – lines 10-17: there is mention of possible geographical variation in coding. It would be informative to know if any variation in the use of various codes was present in the dataset analysed for this paper. |

Page 7 – 'Geographical Variability and Service Provision'. The discussion states that there is variability in admissions between areas, some of which are over three SDs from the directly standardized mean. Looking at the list of PCTs in the supplementary file, it appears that these high admissions outlying areas tend to be in post-industrial northern urban areas. These are often areas with high admissions for all-cause admissions, not just disease-specific. Would the dataset used for this paper allow a calculation of the directly standardized all-cause rates to assess if the high seizures admissions is mirrored by their general behaviour?

Also, within this section it is postulated that deprivation is a potential factor influencing admission rates. Would it be possible to include deprivation as a co-variable in the calculation of a standardized admissions rate?

General points:
The paper would benefit from some discussion around the potential benefits and drawbacks of using the primary diagnosis field only to classify admissions, as against including secondary diagnosis fields. There has been at least one other paper which has explored seizure coding in HES data, also published in BMJ Open (BMJOpen 2016; 6:e010100. doi:10.1136/bmjopen-2015-010100), albeit at regional level, and it would be informative to know if the figures from this paper are comparable. There is a discrepancy between that paper and the current one under review, in the percentage of all-cause admissions for which seizure is responsible.

The aggregation of results at PCT level could make any potential action to be taken in light of this paper difficult to achieve, considering that they have been usurped by CCGs. Whilst there is obviously a difficulty in utilizing a dataset that covers a time period in which the administrative health geography of the country has changed, it would make more sense (if possible) to aggregate the results to that currently used (i.e. CCGs) rather than PCTs.

It is well known that the use of diagnosis codes form the A&E dataset is not robust enough to classify patient cohorts. I am therefore unsure if this part of the paper adds anything to current knowledge.

I have access to several years of HES data myself, although not at a national level, and it is reassuring to see that the prevalence of the seizure and neurology codes mirrors those reported in this paper. However, I have found a larger proportion of dissociative convulsions amongst my cohort. As mentioned above, I think the paper would benefit from an analysis around whether or not there is geographical variation in coding, as well as changes over time.

## VERSION 1 – AUTHOR RESPONSE

**Reviewer: 1**
Reviewer Name: Katherine Hunold
Institution and Country: The Ohio State University, United States of America
Please state any competing interests or state 'None declared': None declared

Please leave your comments for the authors below

The authors utilize a large database in England to describe the healthcare burden by visits for suspected seizures. The manuscript is well-written and figures intentional to display the data in a meaningful way. ***Thanks for reviewing our manuscript and for such positive and helpful feedback. We have responded to each of your points (see red text below) and updated the manuscript accordingly.***

Specific questions and comments are included below:

General:

How should or could these results inform patient care and future investigations? What are the public health implications of these results? What is the applicability of these results outside the UK health system? ***We agree that these are important issues and we have added a new section in the Discussion headed "Implications for Clinical Care and Public Health in the United Kingdom and Internationally" to address them. In terms of future investigations/research we have highlighted these in the revised Discussion (updated in light of your comments).***

Methods:

How did you choose the time period of April 1, 2007 – March 31, 2013? ***We have added the following text to address this point: "Six years of data was judged sufficient to explore readmission rates after the index admission and the cut-off of 31/03/13 was chosen to avoid any potential disruption from 01/04/13 as CCG came into being."***

How many PCTs were excluded when you excluded the top and bottom 10% based on z-score***? 31 PCTs were excluded ie 20% x 151 = 31. We have added this to the manuscript.***

Results / Conclusions:

How do your results for number of ED epilepsy visits and admissions for neurologic conditions compare to previous data? Specifically, when you compare it, does it appear you choose your population correctly? ***The issue of 1) hospital admissions and 2) ED visits are separate. In terms hospital admissions please see our response to Reviewer 2's comment (in blue text) who makes basically the same point. In terms of ED visits, our study is the first that we are aware of in a peer-reviewed journal to report the A&E diagnosis codes. As such it is not possible to compare it to other studies. Reviewer 2 asked, was it worth including the A&E data in the paper? We think that the answer to this is yes. We have concluded (see Discussion section titled 'A&E Data') that the HES A&E data is of poor quality and we think that the lack of good quality diagnostic A&E data is an important issue for service planning and for research in the NHS. Although the low quality of this data seems to be an open secret amongst HES data specialists it is not well known amongst researchers, academics and clinicians. We have added a new sentence to the paragraph in the Discussion to highlight the importance of this issue: "Until the issues with data quality in ED are resolved this will remain an important data-gap which undermines attempts to undertake high quality research, plan services and to evaluate service innovations".***

Are there identifiable drivers for the geographic variability in admissions? ***This is unknown and beyond the scope of our research. Our data-set did not include variables that would allow us to explore this. In the Discussion we have suggested some factors which we think are likely to be important and identified further research as an important next step: "Our research was not designed to investigate potential causes of the variability and the expected or optimal rate of hospital admissions per 100,000 is unknown. Factors which are likely to influence admission rates are the prevalence of epilepsy, deprivation, the quality of ambulatory care and local***

*practice in the emergency care system such as care pathways (including the accessibility of neurological advice) and ED discharge protocols. Further research is required to investigate the causes of the variability demonstrated in this study". Mapping the rates may be helpful to visually identity. We agree that this would be a nice way to illustrate our data but I'm afraid that we don't have the software to accurately draw a map of PCT boundaries and then to highlight the outliers. If so, did you consider geographic weighted regression to test these associations? We have copied and pasted your comment into the text below and answered the question there (Reviewer 2 asked two related questions about geographical clustering).*

Do the PCTs identified as outliers cluster geographically? ***DITTO.***


**Reviewer: 2**
Reviewer Name: Dr Pete Dixon

Institution and Country: Research Associate, University of Liverpool, UK

Please state any competing interests or state 'None declared': None declared

Please leave your comments for the authors below
Thank you for the opportunity to review this interesting paper. ***Thanks for reviewing our manuscript and for such positive and helpful feedback. We have responded to each of your points (see red text below) and updated the manuscript accordingly***. My comments are as follows.

Page 4 – line 54: it would be useful to know the method used to define emergency/unscheduled admissions from the HES in-patient database, i.e. which variable field and which values within it. In addition, it is not clear if the data analysis has been undertaken on episodes or spells, and if the latter, was it the initial episode or the final episode which was used to extract the primary diagnosis? It is not uncommon for the primary diagnosis to change as the spell progresses, so this is an important issue to clarify. ***Thanks for highlighting this, we agree that it is an important issue. We have deleted the original description and replaced it with the following text in the Methods: "We searched the in-patient database for admissions (spells) where ≥1 episode (a period under the care of an individual consultant) during the admission had a primary diagnosis code for a disease of the nervous system."***

Page 5 – lines 19/20: for consistency with the preceding two definitions of searches, it should state if the admissions for dissociative convulsions were on primary diagnosis only. ***We have clarified this as follows: "admissions where the primary diagnosis was dissociative seizures".***

Page 5 – lines 23/24: for clarity it should state from which list the stroke/TIA codes were excluded. ***Stroke/TIA was not included in any of the searches. We have clarified this in the manuscript.***

Page 5 – line 28: from where was the data on costs derived? ***We have added the following to explain how the costs were calculated; "The cost of each A&E attendance was based on: (Health Resources Group (HRG) attributed to each attendance) + (Investigation and Treatment cost) x Market Forces Factor (MFF). The cost of each admission was based on: (HRG attributed to each admission + trim-point (base) cost + Added Bed days cost) x Market Forces Factor (MFF)."***

Page 5 – line 48: "… then PCT that are truly outlying …" should read "… then PCTs that are truly outlying". ***Corrected - thanks.***

Page 6 – lines 21/22: the reporting of the number of dissociative convulsions as a percentage of the

suspected seizures is confusing. As it stands, the wording makes it sound as though the dissociative convulsions code is part of the epilepsy code, when it is made clear in the methods section that it is separate. This should be reworded to avoid any confusion. **Yes, we agree, and we have removed the percentage calculation.**

Page 6 – 'Geographical variability in admissions' section: It is stated that there are five PCTs which are identified as outliers, and refers to the funnel plots in figure C. However, the funnel plots refer to the three separate groups of admission (seizure, neurological conditions and dissociative convulsions), and it is not clear if those PCTs are considered outliers for all, one, or a combination of those conditions. **We have edited the section "Geographical Variability in Admissions" to clarify that it refers to Figure 3a.**

Page 7 – lines 10-17: there is mention of possible geographical variation in coding. It would be informative to know if any variation in the use of various codes was present in the dataset analysed for this paper. **Figure C shows the geographical variability of the diagnoses/codes, the difficulty is that there is no gold standard to compare the ICD-10 codes with ie we don't how the codes relate to the true diagnosis. We have adjusted to manuscript to emphasise this point by adding the following text: "There is evidence that HES diagnostic coding is accurate overall, but there is significant variability amongst the published studies [30]. Research from Canada shows that the diagnosis of epilepsy (G40 and G41) by hospital coders is specific but that the use of R56.8 is required to improve sensitivity – at the cost of reducing overall specificity [31]. There have been no similar studies in the UK looking specifically at seizures/epilepsy i.e. comparing HES ICD-10 diagnosis codes with a gold standard diagnosis."**

Page 7 – 'Geographical Variability and Service Provision'. The discussion states that there is variability in admissions between areas, some of which are over three SDs from the directly standardized mean. Looking at the list of PCTs in the supplementary file, it appears that these high admissions outlying areas tend to be in post-industrial northern urban areas. These are often areas with high admissions for all-cause admissions, not just disease-specific. Would the dataset used for this paper allow a calculation of the directly standardized all-cause rates to assess if the high seizures admissions is mirrored by their general behaviour? **This is an interesting and important point - we have added something to the Discussion to reflect this. Although Health IQ provided the total number of emergency admission per year for the study the actual dataset which we were provided with only included data for neurological conditions and so we cannot analyse all-cause admissions.**

Also, within this section it is postulated that deprivation is a potential factor influencing admission rates. Would it be possible to include deprivation as a co-variable in the calculation of a standardized admissions rate? **I'm afraid that this isn't possible - data on deprivation was not included in our data-set. But we agree that it is an important area for further research and with the correct data (specifically IMD) it should be relatively easy to do - we have included this as a suggestion for further research in the Discussion.**

If so, did you consider geographic weighted regression to test these associations? **All 4 PCTs whose standardised admission rate for suspected seizures were ≥3SDs above the mean are post-industrial northern areas. We don't know of a way to statistically analyse this geographical association but we have added something to the discussion to reflect this observation. We think that an important common factor is likely to be deprivation.**

Do the PCTs identified as outliers cluster geographically? **DITTO.**

General points:

The paper would benefit from some discussion around the potential benefits and drawbacks of using the primary diagnosis field only to classify admissions, as against including secondary diagnosis

fields. *There has been at least one other paper which has explored seizure coding in HES data, also published in BMJ Open (BMJOpen 2016; 6:e010100. doi:10.1136/bmjopen-2015-010100), albeit at regional level, and it would be informative to know if the figures from this paper are comparable. There is a discrepancy between that paper and the current one under review, in the percentage of all-cause admissions for which seizure is responsible.* **We have added a citation to the BMJ Open paper that you mentioned - thanks, this is pertinent to our paper. We have also made direct comparison to this papers Results and our Results. And we have significantly extended the Discussion section headed "In-Patient Admissions for Suspected Seizures" to make comparisons between the two studies.**

The aggregation of results at PCT level could make any potential action to be taken in light of this paper difficult to achieve, considering that they have been usurped by CCGs. Whilst there is obviously a difficulty in utilizing a dataset that covers a time period in which the administrative health geography of the country has changed, it would make more sense (if possible) to aggregate the results to that currently used (i.e. CCGs) rather than PCTs**. Yes, we agree that the change from PCT to CCG is problematic in terms of using our data as a stimulus for change amongst commissioners in CCGs. Our data-set ends on 31/03/13 (range 01/04/07 - 31/03/13) and CCGs came into being on 01/04/13 so our data is purely from PCTs. Although the geographical boundaries of many PCTs were identical to the CCGs that replaced them, some were different, furthermore the initial configuration of CCGs has subsequently changed. To establish which PCTs have identical boundaries to CCGs in 2018 would require a lot of additional work and is beyond the scope of the original project. Accordingly we have not changed the Appendix but we agree that this is an important issue and we have updated the Discussion to include this important issue.**

It is well known that the use of diagnosis codes form the A&E dataset is not robust enough to classify patient cohorts. I am therefore unsure if this part of the paper adds anything to current knowledge. **Yes, it seems to be well known amongst HES experts who regularly use this data and who have a detailed knowledge of it. But we have never seen it presented in a peer-reviewed journal. We think that it is important to demonstrate the weakness of the A&E/ED coding systems and to mention that the Emergency Care Data Set, which has/will supercede it, may only result in a modest improvement in the quality of diagnostic data from A&E/ED. We have added the following text to the DIscussion to emphasise this point: "Until the issues with data quality in ED are resolved this will remain an important data-gap which undermines attempts to undertake high quality research, plan services and to evaluate service innovations."**

I have access to several years of HES data myself, although not at a national level, and it is reassuring to see that the prevalence of the seizure and neurology codes mirrors those reported in this paper. **Thanks for the feedback, consistent with your comments we think that used properly, HES is a very powerful tool for health-services research.** However, I have found a larger proportion of dissociative convulsions amongst my cohort. **We feel that very likely reflects the issue of using primary diagnosis vs secondary diagnoses (as per discussion above).** As mentioned above, I think the paper would benefit from an analysis around whether or not there is geographical variation in coding, as well as changes over time. **As per your comment above ("Page 7 – lines 10-17"), we have adjusted the manuscript to emphasise the problem caused by the absence of a gold standard to compare the ICD-10 codes with i.e. we don't how the codes relate to the true diagnosis. And we have added a citation to the following article which we think is very helpful here: Burns, E.M., et al., Systematic review of discharge coding accuracy. J Public Health, 2012. 34(1): p. 138-48.**

## VERSION 2 – REVIEW

| REVIEWER | Dr Pete Dixon |
| --- | --- |
| | University of Liverpool, UK |
| **REVIEW RETURNED** | 10-Jul-2018 |

| GENERAL COMMENTS | Thank you for the opportunity to review the amended version of this interesting paper. My comments are as follows. |
|---|---|
| | The authors have satisfactorily addressed the issues I flagged in my original review. There are some minor issues re. typos etc. |
| | Results section of abstract – lines 21/22: "… and a very there were a very small number of …". Delete the first "a very". |
| | Geographical variability in admissions section – line 6: "figure 3a shows funnel plots …" should read "figure 3a shows a funnel plot …" |
| | Implications for Clinical care and Public Health etc. section – line 45: "… has much wider determinants that …" should read ""… has much wider determinants than …" |
| | In relation to the comment to reviewer 1's query on mapping the rates, the authors state that they do not have the software to do this. For future work, the authors may find it useful to approach someone who is familiar with producing maps in R or QGIS (both of which are Open Source). However, for the purposes of the current paper, it does appear that PCT boundaries are not readily available, and would require constructing from scratch – which would be a tedious process. |
| | In part of the extra text added to the Discussion section. The authors add in a reference to work by Grainger et al. (for which I am one of the co-authors). They comment that the classification of seizure in the two papers differs in using either primary diagnosis code or primary plus secondary codes. The Grainger paper also only looks at the last episode in spell (i.e. the discharge diagnosis code) rather than >=1 episode with a seizure code as per the current paper. It may be worth highlighting this methodological difference. |
| | In the new text added in the Implications for Clinical care and Public Health etc. section, could a reference be included to back up the assertion that "… research form other European countries shows similar problems with quality of ambulatory care for epilepsy, variability in services and high costs from potentially avoidable admissions"? |

## VERSION 2 – AUTHOR RESPONSE

Reviewer: 2
Reviewer Name: Dr Pete Dixon

Institution and Country: University of Liverpool, UK

Please state any competing interests or state 'None declared': None declared

Please leave your comments for the authors below
Thank you for the opportunity to review the amended version of this interesting paper. My comments are as follows.

The authors have satisfactorily addressed the issues I flagged in my original review. There are some

minor issues re. typos etc. **_We have addressed all the issues below in the revised re-submitted manuscript. Our responses to Reviewer 2's comments are below in red._**

Results section of abstract – lines 21/22: "… and a very there were a very small number of …". Delete the first "a very". **_Done_**.

Geographical variability in admissions section – line 6: "figure 3a shows funnel plots …" should read "figure 3a shows a funnel plot …" **_Done._**

Implications for Clinical care and Public Health etc. section – line 45: "… has much wider determinants that …" should read ""… has much wider determinants than …" **_Done._**

In relation to the comment to reviewer 1's query on mapping the rates, the authors state that they do not have the software to do this. For future work, the authors may find it useful to approach someone who is familiar with producing maps in R or QGIS (both of which are Open Source). However, for the purposes of the current paper, it does appear that PCT boundaries are not readily available, and would require constructing from scratch – which would be a tedious process. **_Yes, we'll bear this in mind for future projects. Thanks for acknowledging that this is not feasible in the current manuscript._**

In part of the extra text added to the Discussion section. The authors add in a reference to work by Grainger et al. (for which I am one of the co-authors). They comment that the classification of seizure in the two papers differs in using either primary diagnosis code or primary plus secondary codes. The Grainger paper also only looks at the last episode in spell (i.e. the discharge diagnosis code) rather than >=1 episode with a seizure code as per the current paper. It may be worth highlighting this methodological difference. **_Done_**.

In the new text added in the Implications for Clinical care and Public Health etc. section, could a reference be included to back up the assertion that "… research form other European countries shows similar problems with quality of ambulatory care for epilepsy, variability in services and high costs from potentially avoidable admissions"? **_Done. I have added citations to Strzelczyk [1] and Begley [2]._**

1.      Strzelczyk, A., et al., *Evaluation of health-care utilization among adult patients with epilepsy in Germany.* Epilepsy Behav, 2012. **23**(4): p. 451-7.
2.      Begley, C.E. and E. Beghi, *The economic cost of epilepsy: a review of the literature.* Epilepsia, 2002. **43**(Suppl 4): p. 3-9.